Agency technical report on the classification and labelling of:

1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylindeno[5,6-*c*]pyran; [galaxolide]; [HHCB]

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Brief summary

The conclusion of the Agency technical report is that 1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylindeno[5,6-c]pyran; [galaxolide]; [HHCB] meets the classification criteria for:

Repr. 1B, H360D (May damage the unborn child)

Is this in agreement with the RAC opinion? YES

At the time of publication, this mandatory classification and labelling (MCL) has not been agreed and/or adopted in Great Britain.

This is a targeted technical report which only considers reproductive toxicity. This was the only hazard class considered in the EU Committee for Risk Assessment (RAC) Opinion.

This substance has an existing MCL which includes Aquatic Acute 1 and Aquatic Chronic 1. Aquatic hazards are not assessed in this technical report, and therefore these classifications should be retained in the GB MCL.

Introduction

Under Article 37 of the GB CLP Regulation[1], the Agency[2] is required to produce a technical report for each substance on which the Committee for Risk Assessment (RAC) of the European Chemicals Agency produces an opinion[3].

This technical report documents an independent scientific assessment, conducted by HSE technical specialists, of the classification and labelling of 1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylindeno[5,6-c]pyran; [galaxolide]; [HHCB].

Table 1. Information considered in the scientific assessment

Document	Included in assessment
EU CLH report	Yes
Annexes to the EU CLH report	Yes
RAC opinion	Yes
Background document	Yes
Information submitted during the EU public consultation process (RCOM table, including attachments)	Yes
RAC minority opinion(s)	Not applicable
Other information:	No

This information has been evaluated against the classification and labelling criteria set out in the GB CLP Regulation.

[1]The retained CLP Regulation (EU) No. 1272/2008 as amended for Great Britain

[2] HSE acting in its capacity as the GB CLP Agency

[3] Under Article 37(4) of Regulation (EU) No 1272/2008 on classification, labelling and packaging of substances and mixtures

Overview of current and proposed classification and labelling

Table 2. Current and proposed classification and labelling

	Index No.	International Chemical Identification	EC No.	CAS No.	Classification		Labelling			Specific Concentration Limits, M-factors	Notes
					Hazard Class and Category Code(s)	Hazard Statement Code(s)	Pictogram, Signal Word Code(s)	Hazard Statement Code(s)	Suppl. Hazard Statement Code(s)		
GB MCL List entry	603-212-00-7	1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylindeno[5,6-c]pyran; [galaxolide]; [HHCB]	214-946-9	1222-05-5	Aquatic Acute 1 Aquatic Chronic 1	H400 H410	GHS09 Wng	H410			
EU dossier submitter's proposal	603-212-00-7	1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylindeno[5,6-c]pyran; [galaxolide]; [HHCB]	214-946-9	1222-05-5	**Add** Repr. 1B	**Add** H360Df	**Add** GHS08 **Modify** Dgr	**Add** H360Df			
EU RAC opinion	603-212-00-7	1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylindeno[5,6-c]pyran; [galaxolide]; [HHCB]	214-946-9	1222-05-5	**Add** Repr. 1B	**Add** H360D	**Add** GHS08 **Modify** Dgr	**Add** H360D			
Agency technical report conclusion	603-212-00-7	1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylindeno[5,6-c]pyran; [galaxolide]; [HHCB]	214-946-9	1222-05-5	**Add** Repr. 1B	**Add** H360D	**Add** GHS08 **Modify** Dgr	**Add** H360D			
Resulting MCL entry on GB MCL list	603-212-00-7	1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylindeno[5,6-c]pyran; [galaxolide]; [HHCB]	214-946-9	1222-05-5	Repr. 1B Aquatic Acute 1 Aquatic Chronic 1	H360D H400 H410	GHS08 GHS09 Dgr	H360D H410			

Background

Active substance in Plant Protection Products: ☐

Active substance in Biocidal Products: ☐

Chemical registered under REACH: ☒

1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylindeno[5,6-*c*]pyran is also known as galaxolide, HHCB and Musk 50, and is referred to in this report as HHCB. It is a polycyclic musk used for washing and cleaning products, biocides (e.g. disinfectants, pest control products), air care products, polishes and waxes, perfumes and fragrances, cosmetics and personal care products (CLH, 2024).

It is a clear, colourless, viscous liquid with the following structure:

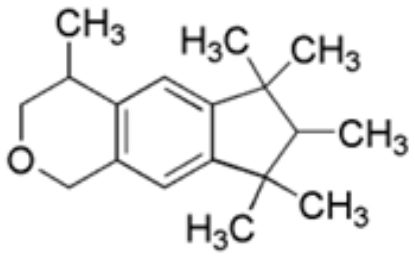

Figure 1: chemical structure of HHCB, extracted from the EU RAC opinion (ECHA, 2026)

Scientific assessment of the physical, human health and environmental hazard classes

Physical Hazards

Not assessed in the CLH report or RAC opinion.

Health Hazards

Acute Toxicity

Not assessed in the CLH report or RAC opinion.

Specific target organ toxicity – single exposure (STOT SE)

Not assessed in the CLH report or RAC opinion.

Skin corrosion/irritation

Not assessed in the CLH report or RAC opinion.

Serious eye damage/irritation

Not assessed in the CLH report or RAC opinion.

Respiratory sensitisation

Not assessed in the CLH report or RAC opinion.

Skin sensitisation

Not assessed in the CLH report or RAC opinion.

Specific target organ toxicity – repeated exposure (STOT RE)

Not assessed in the CLH report or RAC opinion.

Germ cell mutagenicity

Not assessed in the CLH report or RAC opinion.

Carcinogenicity

Not assessed in the CLH report or RAC opinion.

Reproductive toxicity

Classification agreed by RAC:

Adverse effects on sexual function and fertility

For consideration of the potential effects of HHCB on sexual function and fertility, a simplified screening study used as a dose range finding study for an Extended One-Generation Reproductive Toxicity Study (EOGRTS) and an EOGRTS were available.

Dose range-finder, non-guideline (based on OECD TG 421), Wistar rats

In the dose range-finder, groups of Wistar rats (10/sex/dose) were administered HHCB via the diet at concentrations of 690 and 2480 ppm for males and 305, 690 ppm and 1090-2480 ppm for females; corresponding to 34-47 and 121-168 mg/kg bw/d for males and 38-71 and 134-257 mg/kg bw/d for females. Females were exposed for 13 weeks in total, beginning with a 2-week pre-mating period, and continuing through mating, gestation and lactation until lactation day (LD) 21. Males were dosed for 29 days, beginning with the 2-week pre-mating period. The following deviations from OECD TG 421 were noted: the use of only two dose levels, missing parameters from the historical control data (HCD), histological examination only being performed on the kidneys, no measurements provided for anogenital distance (AGD), lack of haematology and clinical biochemistry, no reporting on hormones and no statistical analysis. There was no concurrent control group as part of this study. There were no mortalities or clinical signs of toxicity. No differences in food consumption or body weight were identified between the two dosed groups.

Effects on organ weights were noted in the liver, kidney and thyroid. In the liver, relative weights were increased by ↑ 33%/25% (M/F), and ↑ 48%/51% (M/F) at the low and high dose respectively. In the kidney, relative weights were increased by ↑ 16%/9% (M/F) and ↑ 17%/16% (M/F) at the low and high dose when compared with the available HCD. In the thyroid, relative weights were increased in males; ↑ 15% and 64% in the low and high dose respectively. In females, there was a 64% increase in thyroid weight at the top dose only. Statistical significance cannot be confirmed, as no statistical analysis was conducted.

There was no effect on the oestrous cycle.

At the top dose, 1 couple failed to mate. There were 10 and 9 pregnant females in the low and high dose groups, respectively, with no apparent effects on gestation length, implantation, pre-birth loss, numbers of pups delivered or numbers of live pups.

Sperm analysis showed no difference between groups in the mean sperm count in testes, and no difference in the cauda epididymis weight. The mean number of sperm in samples from a fragment of the cauda epididymis was 30% lower in the high dose compared to the low dose. There were no differences in sperm motility or morphology.

RAC concluded that the dose range finder study was of limited usefulness, based on its deviations from OECD TG 421.

Extended One Generation Reproductive Toxicity Study, OECD TG 443, Wistar rats

The simplified screening study described above was used as a dose range-finder for an EOGRTS, which was conducted with cohorts 1A, 1B and 1C but without developmental immunotoxicity or developmental neurotoxicity cohorts. Cohort 1B was used to produce the F2 generation. In the F0 generation, groups of 25 Wistar rats/sex/dose were administered HHCB via the diet at concentrations of 470, 825 and 1650 ppm, equating to 42.5, 75 and 150 mg/kg bw/d. The control group received a basic diet. Animals in the F0 generation were dosed for 10 weeks before mating, throughout mating and through to necropsy (16 weeks total, including through gestation and at least 21 days after parturition in females). Animals in the F1 generation (20/sex/cohort) were not dosed directly through the lactation period up to post-natal day (PND) 21, but after weaning on PND 22, received the test substance via the diet at the same nominal doses as the F0 generation until the day before or day of scheduled necropsy (in cohort 1B; at least 20 weeks for males and at least 19 weeks for females). F2 pups were not dosed directly with the test substance.

In F0 animals, there were no mortalities and no clinical signs of systemic toxicity or effects on food consumption or body weight.

There was a statistically significant increase in relative liver weight in most treated groups: ↑ 7 % (females only), ↑ 7%/3% (M/F) and ↑ 15%/8% (M/F) at the low, mid and top dose respectively.

In the thyroid, there was a statistically significant increase in relative weights for top dose males and all treated females. These were ↑ 21%, ↑ 16% (females only, low and mid dose respectively) and ↑ 18%/28% M/F (top dose). These findings were accompanied by histopathological findings at the top dose: follicular cell hypertrophy in 5/25 males (minimal) and 5/25 females (minimal to mild). Clinical chemistry also showed a statistically significant decrease in T4 hormones in males only, by ↓24.8% and ↓26.25% in the mid and top dose respectively.

At the top dose, there was a statistically significant increase in the number of animals with an acyclic oestrous cycle, this was 24% compared with 8% in control animals.

There were no effects on mating, fertility or gestational indices or gestational duration. Sperm analysis showed no effect.

A slight, dose-dependent decrease in the number of implantation sites was noted, with mean numbers of 12.8, 12.6 and 12.3 at the low, mid and top dose respectively, compared with 13.3 in concurrent controls. This was not statistically significant and was within the HCD range of 10.2-15.0 listed in the CLH report[4]. Therefore, RAC could not determine whether this effect was related to treatment with HHCB. The decrease in implantation sites did not affect the number of pups born per litter.

There was a statistically significant decrease in absolute epididymis and seminal vesicle weights at the top dose only: ↓7% compared to the control. Relative weights were unaffected and there were no associated histopathological changes.

In the F1 generation, there were no mortalities or clinical signs of systemic toxicity in treated animals. RAC noted a statistically significant reduction in food consumption in all treated groups, along with reductions in body weight on PND 21(↓6.4% and 11% at the mid and top doses respectively). Mean body weights were also lower at study termination, with statistically significant reductions of 8%, 11% and 17% in cohort 1B males at the low, mid and top doses, and 7% in top-dose cohort 1B females.

There was a statistically significant increase in relative liver weights at the top dose in cohorts 1A and 1B. In cohort 1A, there was a ↑ 20% increase in males only and in cohort 1B there was a ↑ 11%/9% (M/F) increase. There were also statistically significant increases in relative thyroid weights in both cohorts. In cohort 1A these were ↑ 25% (males only), ↑ 30% (males only) and ↑44%/15% (M/F) in the low, mid and top doses respectively. In cohort 1B, these were ↑ 13% (males only) and ↑ 25%/24% (M/F) in the mid and top doses respectively.

There was no effect on the oestrous cycle. Mating, fertility and gestational indices and gestational duration were not affected. Sperm analysis showed no findings.

There was a statistically significant decrease in absolute epididymis weights for all treated males: ↓ 8%, 7%, and 12% in cohort 1A and ↓ 5%, 8% and 12% in cohort 1B for the low, mid and top dose respectively.

There was a statistically significant decrease in absolute prostate weight in cohort 1A males: ↓ 10% and 11% at the mid and top doses respectively. There was also a statistically significant decrease in absolute seminal vesicle weights in top dose males in the same cohort of ↓ 12%. Absolute testis weights were decreased in top dose males in both cohorts: ↓ 8% in cohort 1A and ↓ 7% in cohort 1B.

In F1 animals at the top dose, the mean number of implantation sites was statistically significantly reduced by 7.5% (11.3 compared to 12.5 in the control group), though RAC

[4] The RAC opinion notes that the HCD described in the CLH report for this finding differs from those described in the Appendix of the EOGRTS report. This study report is not available to the Agency.

noted that this was within the HCD range (11.0-12.8, mean = 12.2). As a result, the mean number of pups delivered per litter was reduced (10.7 compared to 11.6 in the control); this value was within the HCD range (9.9-11.8, mean = 11.1) and the decrease was not statistically significant. Balano-preputial cleavage occurred later in all treatment groups compared to the control group (50.0, 52.5, 52.4 and 51.5 days in the control, low, mid and top dose groups, respectively); this finding was statistically significant but occurred without a clear dose-response relationship.

Comparison with CLP criteria

Adverse effects on sexual function and fertility are defined as “any effect of substances that has the potential to interfere with sexual function and fertility. This includes, but is not limited to, alterations to the female and male reproductive system, adverse effects on onset of puberty, gamete production and transport, reproductive cycle normality, sexual behaviour, fertility, parturition, pregnancy outcomes, premature reproductive senescence, or modifications in other functions that are dependent on the integrity of the reproductive systems” (Annex I, Section 3.7.1.3 of the CLP Regulation).

Substances may be considered for classification in Category 2 “when there is some evidence from humans or experimental animals, possibly supplemented with other information, of an adverse effect on sexual function and fertility, or on development, and where the evidence is not sufficiently convincing to place the substance in Category 1. If deficiencies in the study make the quality of evidence less convincing, Category 2 could be the more appropriate classification.” Such effects shall have been observed in the absence of other toxic effects, or if occurring together with other toxic effects the adverse effect on reproduction is considered not to be a secondary non-specific consequence of the other toxic effects” (Table 3.7.1 (a) of the CLP Regulation).

Overall, RAC concluded that the observed changes in male reproductive organ weights in the EOGRTS did not warrant classification, as they were small in magnitude (up to 12%) and were limited to absolute weights with inconsistent increases relative to body weight. There were no changes relative to brain weight. Additionally, no dose-response relationship or associated histopathological findings could be identified.

The slight reduction in the mean number of implantation sites in the F1 generation (11.3 compared with 12.5) was within HCD. The acyclicity observed was restricted to the parent generation.

Doses in this study were equivalent to 42.5, 75 and 150 mg/kg bw/d. No mortalities or clinical signs of toxicity were observed in the above dose range finder (up to 257 mg/kg bw/d in top dose females). RAC concluded that the top dose of 150 mg/kg bw/d could have been higher, based on the results of the dose range-finding (DRF) study.

Overall, RAC concluded that classification for sexual function and fertility was not warranted.

Adverse effects on development

For consideration of the developmental toxicity potential of HHCB there were 8 studies available. These were 2 developmental toxicity studies in rats and rabbits, along with their respective dose range-finding studies, one tolerability study in rabbits, and a peri/postnatal developmental neurotoxicity test in rats. The EOGRTS and simplified screening study described in the sexual function and fertility section were also considered.

Dose range-finder study, OECD 414, SD rats, 1997b

In this study, 8 pregnant SD rats/group were administered HHCB in corn oil at doses of 100, 250, 500 or 1000 mg/kg bw/d by oral gavage. Administration took place on gestation day (GD) 7-17, and a control group of 19 pregnant rats were administered corn oil only.

In the top dose group (1000 mg/kg bw/d) 3 rats died on days 10, 10 and 12. There was a decrease in maternal body weight gain during the treatment period compared with concurrent controls: ↓ 5% and ↓ 12.2% at 500 and 1000 mg/kg bw/d respectively.

Dams in the top dose group of 1000 mg/kg bw/d were found to have pups with reduced body weight (↓ 11%).

Regarding foetal gross external alterations, one foetus in the control group had a thread-like tail. One foetus had micrognathia, low set ears and spina bifida at 500 mg/kg bw/d.

Prenatal Developmental Toxicity (PNDT) Study, OECD TG 414, SD rat 1997a

Groups of 25 female SD rats/dose were administered HHCB at doses of 50, 150 and 500 mg/kg bw/d via oral gavage. A control group was included and received 5 mL/kg bw/d corn oil. Exposure was from GD 7-17 only, not up to GD 20 in line with the current OECD TG 414. However, the test was conducted in line with the 1981 version of OECD TG 414 and was GLP-compliant. No specific data on the purity of the substance was available.

In the dams, there were no mortalities. Top dose animals showed clinical signs of toxicity including 9 with excess salivation, 7 with urine-stained abdominal fur, 4 with red or brown substance on the forepaws and 6 with alopecia. There was a decrease in body weight at GD 20: ↓ 2.5%, 3.3% and 4.8% at 50, 150 and 500 mg/kg bw/d respectively. This was statistically significant at the mid and high doses. The DS noted that at GD0, the body weight of all dose groups compared to control were already statistically significantly lower (by 3.6, 3.8 and 3.3%, respectively). Corrected body weights at GD20, as calculated by DS were not statistically significantly different. There was a statistically significant decrease in feed consumption of ↓ 11.1% at the top dose only. Decreases in food consumption (not

statistically significant) were noted in the low and mid dose groups (3.5 and 4.4%, respectively).

There were no dose-dependent or statistically significant differences in the litter sizes, number of live/dead foetuses, early or late resorptions, and there were no dead foetuses.

There was a statistically significant increase in structural abnormalities in the foetuses. RAC listed the following:

Text copied from pages 13-14 of the RAC opinion (ECHA, 2026)

- Control group:

One foetus had micrognathia and an oedematous body (anasarca). Soft tissue examination revealed absent tongue, interventricular septal defect in the heart with transition of the great vessels, situs inversus of the liver, spleen, intestines, pancreas, stomach and kidneys, and malformed lungs.

- 50 mg/kg bw/d:

No malformed foetuses.

- 150 mg/kg bw/d:

One foetus had a kinked tail.

One foetus had interrelated head malformations indicative of microcephaly (small head, small, low set (ectopic) ears, absent eye bulges and upper and lower jaws and a smaller oral opening) and an umbilical hernia. Soft tissue examination of this foetus revealed additional head malformations associated with microcephaly (microphthalmia of both eyes, absence of nasal passages, tongue and lateral ventricles of the brain and moderate dilation of the fourth ventricle in the brain).

- 500 mg/kg bw/d:

One foetus had a short trunk and a thread-like tail

One foetus had depressed eye bulges and a domed head. Skeletal examination revealed the expected skull malformation (small eye sockets), retarded ossification or possible malformation (shortening) of the nasals, maxillae and premaxillae, moderate enlargement of the anterior fontanelle, small scapulae and interrelated vertebral/rib malformations.

One foetus had skull malformations (short, fused mandibles and micrognathia), a thoracic vertebral malformation and retarded ossification of the sternum.

One foetus had micrognathia and a small tongue.

One foetus had a thoracic vertebral malformation.

And a littermate of the latter had a depressed left eye bulge with associated microphthalmia.

End of copied RAC text

The Agency submitted a comment requesting further information on the origin of the HCD and a percentage range/mean for the incidence (foetal and litter) of each finding as part of RAC's public consultation. The DS reported that HCD were available from studies conducted on CD rats between June 1994 and June 1996. The exposure routes used in these studies were not specified.

No findings were reported in the HCD for microcephalia, small ears, an absent jaw, absent eye bulges, an absent or small tongue or domed head. Findings of microphthalmia and micrognathia were reported, with foetal and litter incidences of 0-1. Depressed eye bulges were also reported, with foetal incidences of 0-2 and litter incidences of 0-1.

In the OECD TG 414 study, there were also statistically significant increases in the foetal incidence of incomplete ossification and/or no ossification of sternal centra (5.4% of foetal incidence compared to 0.5% in the control group; 23.8% of litter incidence compared to 4% in the control group) and a small, though statistically significant, decrease in the number of ossification sites in the metatarsals (mean of 3.98 compared to 4.00 in all other groups) seen at 500 mg/kg bw/d.

There was also a statistically significant increase in skeletal alterations. This included foetal incidences of thoracic vertebral malformations (hemivertebrae and centrum fused). In the top dose group, accompanied by rib alterations were found in 3 foetuses from 3 different litters (foetal incidence of 2%, litter incidence 14.3% compared to 0/0 in the control group). These were not reported in the HCD.

In conclusion, at the highest dose, increased incidences of craniofacial (interrelated-skull) and vertebral/rib malformations and growth retardation (reduced pup weight and delayed ossification) were observed in the absence of severe maternal toxicity in rats. RAC noted that the overall incidence of malformations increased at the top dose compared to other groups, with foetal/litter incidences of 1/1, 0/0, 2/2 and 5/6 at 0, 50, 150 and 500 mg/kg bw/d, respectively.

Dose range finding study (non-guideline) New Zealand White (NZW) rabbits, unpublished study report 2020c

In this non-guideline dose range-finding study, groups of 6 pregnant NZW rabbits/group were administered 0, 30, 100 and 300 mg/kg bw/d of HHCB in corn oil by oral gavage; with a total dose volume of 4ml/kg from GD6 to GD9 and 2ml/kg from GD10 to GD28.

One female in the top dose group was found dead on GD 23. There were no treatment-related effects on clinical signs, body weight or food consumption. There was some maternal toxicity in animals in all groups including the controls described by RAC as negligible food consumption leading to body weight loss. Dosing led to the death or premature euthanasia of 1, 2, 3 and 3 females in the control, 30, 100 and 300 mg/kg/d groups, respectively. These deaths were considered to be caused by vehicle-related maternal toxicity, which included negligible food consumption leading to body weight loss, rather than a toxic effect of HHCB.

There was an increase in absolute/relative kidney and liver weights in all treated groups compared to the control.

In the liver, relative weights were ↑ 26%, ↑ 28%, and ↑ 50% at 30, 100 and 300 mg/kg bw/d. In the kidney, relative weights were ↑ 13%, ↑ 19%, and ↑ 32% at 30, 100 and 300 mg/kg bw/d respectively. Relative weight increases were statistically significant at the top dose.

There was a lower mean absolute gravid uterus weight at 30 and 300 mg/kg/d (405 g and 400 g, respectively) when compared with the concurrent control (490 g) and with the HCD mean (552g). There was a statistically significant decrease in the relative gravid uterus weight at the low and high doses (↓16% and ↓15% at 30 and 300 mg/kg/d, respectively).

The number of implantations decreased ↓ 10% and ↓10% at 30 and 300 mg/kg bw/d, but the change was not statistically significant. The rate of post-implantation losses was higher than the concurrent control and HCD mean after treatment, with increases of ↑ 440% and ↑ 548% at 30 and 300 mg/kg/d. Therefore, the mean number of live foetuses was decreased in all treated groups, with 8.7, 9.0 and 7.7 at 30, 100 and 300 mg/kg/d, respectively.

RAC noted that the increased post-implantation loss observed at 30 and 300 mg/kg bw/d in this preliminary study was not reproduced in the main study (2020b, described below). Several factors may explain the observed discrepancies in the results. One potential factor is the limited sample size: only three animals per dose group were assessed at the 30 and 300 mg/kg bw/d doses, owing to the mortality described above. Additionally, the highest dose of 300 mg/kg bw/d was not tested in the main study.

Maximum Tolerated Dose study, NZW rabbits, unpublished study report, 2020d

In this non guideline MTD study, HHCB was administered at levels of 300 mg/kg bw/d by oral gavage for 8 days. A corn oil vehicle was used, and the total dose volume was 1.25 mL/kg/d. The treatment group consisted of 3 non-pregnant NZW rabbits. One concurrent control group received corn oil only.

The DS noted that maternal toxicity was more severe with HHCB administered at 300 mg/kg bw/d compared with administration with corn oil only at a dose volume of 1.25 mL/kg/d. The nature of this toxicity was not described or quantified.

Following a 9-day recovery period, 4 animals (1 from the control and 3 from the treatment group) received a dose volume of 0.8 mL/kg/d of corn oil for 5 days, followed by dosing with HHCB at 100 mg/kg/d for 8 days. There was no clear maternal toxicity and no clear differences in effects between the 100 mg/kg bw/d and corn oil only animals.

Based on these findings, a dose of 100 mg/kg bw/d and a dose volume of 0.8 mL/kg bw/d of corn oil, was considered appropriate as a high dose for subsequent studies in the pregnant rabbit.

PNDT study OECD TG 414, unpublished study report, 2020b

Dose levels for this study were selected based on a dose range-finding prenatal developmental toxicity study (DRF-study) in the rabbit and a tolerability study in the non-pregnant rabbit (MTD-study).

Groups of 22 pregnant NZW rabbits/dose were administered HHCB at doses of 0, 10, 30 and 100 mg/kg bw/d via oral gavage. Exposure was from GD 6 to GD 28. The study was conducted in line with OECD TG 414 and was GLP compliant.

In the mid dose group (30 mg/kg bw/d) 1 animal died, and 4 animals also died in the top dose group, though RAC noted that one of these deaths was attributed to a gavage error. The mid dose females had a marked decrease in food consumption and associated body weight loss of ↓ 14%. In the top dose group, 2 of the females were euthanised after a marked decrease in food consumption and associated body weight loss of approximately ↓ 20%. The third animal that died in the top dose group showed a 25% body weight loss from GD 12-27 and was euthanised on day 27. The study authors considered the effects leading to euthanasia of the 3 dams in the high dose group and 1 dam in the mid dose group as an exacerbation of vehicle-related effects by the test item. However, RAC noted that vehicle-related clinical signs (reduced faecal output, pale or soft/small faeces and absent urine) were comparable between the control and treated groups.

In terms of viability, mean live litter sizes in treated groups were comparable or higher when compared with controls; 9.6, 10.3, 9.6 and 9.2 in controls, 10, 30 and 100 mg/kg bw/d respectively. Total resorptions were comparable or lower than concurrent controls; 0.7, 1.0, 0.5 and 0.6 in controls, 10, 30 and 100 mg/kg bw/d respectively. Low mean foetal weight was noted in all groups including controls when compared with HCD. The study authors considered this to be related to the corn oil vehicle rather than an effect of HHCB exposure.

Table 3: mean live foetal body weight of NZW rabbit foetuses, from Table 34 of the CLH report (CLH, 2024)

	Control 0 mg/kg bw/d	10 mg/kg bw/d	30 mg/kg bw/d	100 mg/kg bw/d	HCD*
Live foetal body weight (g)	32.68	35.60	37.22	34.11	40.90

** HCD obtained from 23 studies performed in 2018*

Structural malformations were noted in some of the foetuses. In the control group, fused sternebrae, characterised as severe was noted in 2 animals in separate litters, and one animal in another litter had multiple skeletal malformations (forelimbs, hindlimbs and ribs large and short). In the low dose group (10 mg/kg bw/d) one foetus had kidney malformations consisting of caudal malposition fusion on the midline, as well as severe sternoschisis. This was the only foetus with structural abnormalities in the low dose group. In the mid dose group (30 mg/kg bw/d), malformations were observed in 4 foetuses from different litters. Gastroschisis and sternoschisis occurred in one foetus, and omphalocele occurred in another. Another foetus had fused lung lobes and a retroesophageal right subclavian artery. The fourth foetus had a dilated aortic arch, ventricular septal defect in the heart and a narrowed pulmonary trunk. In the top dose group, one foetus had omphalocele and another from a different litter had a malrotated hindlimb, cleft palate, small tongue, malpositioned kidneys, retroesophageal right subclavian artery and fused sternebrae characterised as severe.

The foetal incidence of individual malformations is shown in the table below:

Table 4: foetal incidence of external, skeletal and visceral malformations in rabbit pups, adapted from tables 36, 37 and 38 of the CLH report (CLH, 2024)

Dose level (mg/kg bw/d)	0 (control group)	10	30	100	HCD
Gastroschisis	0/202	0/186	1/144 (0.69%)	0/157	1/5480 (0.02%)
Omphalocele	0/202	0/186	1/144 (0.69%)	1/157 (0.60%)	7/5480 (0.13%)
Malrotated hindlimb	0/202	0/186	0/144	1/157 (0.60%)	2/5480 (0.04%)

Dose level (mg/kg bw/d)	0 (control group)	10	30	100	HCD
Cleft palate	0/202	0/186	0/144	1/157 (0.60%)	None
Small tongue	0/96	0/88	0/69	1/75 (1.18%)	None
Fused sternaebrae (severe)	2/202 (1.16%)	0/186	0/144	1/157 (0.59%)	None
Sternaebra, severe sternoschisis	0/202	1/186 (0.40%)	0/144	0/157	None
Sternaebra, sternoschisis	0/202	0/186	1/144 (0.69%)	0/157	None
Multiple skeletal malformations (forelimbs, hindlimbs and ribs large and short)	1/202	0/186	0/144	0/157	Not reported
Malpositioned kidneys, caudally and fused on midline	0/202	1/186 (0.40%)	0/144	1/157	2/4635 (0.04%)
Fused lung lobes	0/202	0/186	1/144	0/157	None
Retroesophageal right subclavian artery	0/202	0/186	1/144	1/157	7/4635 (0.15%)
Dilatated aortic arch	0/202	0/186	1/144	0/157	None
Ventricular septal defect (heart)	0/202	0/186	1/144	0/157	2/4635 (0.04%)
Narrowed pulmonary trunk	0/202	0/186	1/44	0/157	None

Extended One Generation Reproductive Toxicity Study (EOGRTS), OECD TG 433, Wistar rats, 2021

See sexual function and fertility section for more details on the study design and information on systemic toxicity.

The EOGRTS was conducted with cohorts 1A, 1B and 1C but without DIT/DNT cohorts. Cohort 1B was used to produce the F2 generation.

In the F0 generation, groups of 25 Wistar rats/sex/dose were administered HHCB at doses of 470, 825 and 1650 ppm, equating to 42.5, 75 and 150 mg/kg bw/d. The control group received a basic diet. Animals in the F0 generation were exposed via the diet for 10 weeks before mating, throughout mating and through to necropsy (16 weeks total, including through gestation and at least 21 days after parturition in females). Animals in the F1 generation (20/sex/cohort) were not dosed directly through the lactation period up to PND 21, but after weaning on PND 22, received the test substance via the diet at the same nominal doses as the F0 generation until the day before or day of scheduled necropsy (in cohort 1B; at least 20 weeks for males and at least 19 weeks for females). F2 pups were not dosed directly with the test substance.

In F0 animals, there were no mortalities and no clinical signs of systemic toxicity or effects on food consumption or body weight.

There were no effects on F1 postnatal survival in any group. The mean number of pups delivered was comparable with that of the control group in all treated groups. There was no effect of treatment on live birth index, viability index and lactation index. Sex-ratio, anogenital distance and areolae/nipple retention were not affected. There were no clinical signs during lactation. Mean F1 pup body weight was decreased by 8% at the top dose compared to the control (see Table 5 below).

In the F2 generation, there was a statistically significant dose-related decrease in F2 pup body weight during lactation (see Table 5 below). Also during lactation, the mean body weight of the F1 dams was statistically significantly lower.

Table 5: postnatal mean pup body weights from the EOGRTS (statistical significance indicated in bold)

Dose	Control	42.5 mg/kg bw/d	75 mg/kg bw/d	150 mg/kg bw/d
F1 generation				
PND 1	6.63±0.84	6.40±0.55	6.27±0.74	**6.10±0.83* (-8%)**
PND 4	10.19±1.72	10.09±1.06	9.66±1.66	**9.31±1.37* (-9%)**
PND 7	16.70±2.14	16.28±1.34	15.79±1.97	**15.18±2.24** (-9%)**
PND 14	33.76±3.11	32.30±2.02	31.64±3.00	**29.94±2.08*** (-11%)**
PND 21	55.04±4.47	53.56±2.76	**52.21±4.24** (-5.1%)**	**49.06±3.19*** (-11%)**

Dose	Control	42.5 mg/kg bw/d	75 mg/kg bw/d	150 mg/kg bw/d
F2 generation				
PND 1	6.55±0.75	6.60±0.71	6.40±0.71	6.56±0.44
PND 4	10.26±1.38	10.32±1.52	9.90±1.24	9.94±0.63
PND 7	16.87±2.08	16.87±1.78	**16.09±1.72* (-5%)**	**15.68±0.95** (-7%)**
PND 14	34.43±2.52	33.83±2.45	**31.85±2.85*** (-7%)**	**29.98±1.80*** (-13%)**
PND 21	55.60±3.55	55.15±4.56	**51.84±4.74** (-7%)**	**49.48±2.59*** (-11%)**

** test: Shirley 2-sided p<0.001 or Williams 2-sided p<0.05, ** test: Williams 2-sided p<0.01, *** test: Williams 2-sided p*

AGD, presented as AGD per cube root of body weight, decreased at the top two doses. Statistics for the F1 and F2 generations were recalculated from the raw data by the DS, after they highlighted a typographical error in the final study report. The DS did not identify any statistically significant results for the F1 generation. For the F2 generation, a statistically significant dose-related decrease in AGD from the mid-dose for males (means of 2.0 and 1.9) and for females (mean of 1.0 and 0.9) was observed compared to the control group (means of 2.4 and 1.2 for males and females, respectively). RAC noted that the mean AGD values in F2 animals at the mid and top doses, whilst statistically significantly lower, fell in the middle of the HCD range, whilst the values for the control and low dose group were at the upper end or slightly above the HCD range. Additionally, they noted that anti-androgenic effects would be expected to cause decreased AGD in males and increased AGD in females, which was not the case in the EOGRTS. Based on these considerations, RAC could not attribute the changes in AGD solely to treatment with HHCB and therefore concluded that this effect was of limited relevance to the assessment of developmental toxicity.

While no changes were found in the F0 generation, a statistically significant decrease in absolute testis weight was noted in F1a and F1b at the top dose; ↓ 3.35% and ↓ 3.77% respectively. Relative (to body weight) testis weights were increased from the mid dose in both groups; ↑ 1.11% and ↑ 1.12% in F1a and ↑ 0.93% and ↑ 0.96% in F1b respectively. No statistically significant changes were found in testis relative to brain weight. However, since this was a relatively limited effect, and is not supported by histopathological findings, RAC did not consider this relevant for classification.

Simplified reproduction/developmental toxicity screening study (used as DRF for EOGRTS), 2020a

Groups of 10 Wistar rats/dose were administered HHCB at doses of 690 and 2480 ppm for males and 305, 690 ppm and 1090-2480 ppm for females; corresponding to 34-47 and 121-168 mg/kg bw/d for males and 38, 71 and 134-257 mg/kg bw/d for females. Animals were exposed for 13-weeks total, including a 2-week pre-mating period every day via the diet. There was no concurrent control group as part of this study.

There were no mortalities or clinical signs of toxicity, or effects on food consumption or body weight in any dosed groups.

Further information on systemic toxicity can be found in the sexual function and fertility section.

There was a dose-related decrease in mean pup body weights in both males and females at the highest dose compared with the HCD. The magnitude of the change was up to 12% in males and 10% in females at 2480 ppm compared to HCD at PND21. Due to the absence of a control group, no statistical analysis was performed.

Peri/postnatal developmental neurotoxicity test, CD rats, unpublished study report, 1996

This study was based on guidelines endorsed by the ICH Steering Committee on the Detection of Toxicity to Reproduction for Medicinal Products. It was GLP-compliant and designed to determine the effects of HHCB on neonates when exposed through nursing. Groups of 28 female CD rats/dose were administered HHCB at 0, 2, 6 or 20 mg/kg bw/d once daily by gavage in corn oil. The total dose volume was not available. HHCB was administered from GD 14 to PND 21. Groups of 24 male and female pups per dose were retained to maturity and assessed for behavioural changes (accelerating rotarod test, Actimat test, passive avoidance test) and reproductive capacity. At 84 days of age, animals in the F1 generation were mated to produce the F2 generation. F2 animals were examined at parturition and periodically until PND 21, at which point the study was terminated.

RAC noted that no adverse effects were observed during pregnancy or lactation. No effects were apparent on development of the F1 generation during the late prenatal phase, or on postnatal growth, no changes in post-weaning behavioural or mating performance were seen and post-mortem examination of F1 males and females, reproductive capacity, litter data and macroscopic post mortem examination of F2 pups did not reveal abnormalities.

No data were available on these parameters. RAC noted that the doses used in this study could have been higher.

Comparison with the classification criteria

Adverse effects on development are considered as “any effect which interferes with normal development of the conceptus, either before or after birth, and resulting from exposure of either parent prior to conception, or exposure of the developing offspring during prenatal development, or postnatally, to the time of sexual maturation. However, it is considered that classification under the heading of developmental toxicity is primarily intended to provide a hazard warning for pregnant women, and for men and women of reproductive capacity. Therefore, for pragmatic purposes of classification, developmental toxicity essentially means adverse effects induced during pregnancy, or as a result of parental exposure. These effects can be manifested at any point in the life span of the organism. The major manifestations of developmental toxicity include (1) death of the developing organism, (2) structural abnormality, (3) altered growth, and (4) functional deficiency” (Annex I, Section 3.7.1.4 of the CLP Regulation).

Death of the developing organism

In the DRF study on NZW rabbits (ref: 2020c) there were a total of 9 mortalities, spanning all groups of the study including controls. Maternal toxicity was characterised as negligible food consumption leading to body weight loss linked the death or premature euthanasia of 1, 2, 3 and 3 females in the control, 30, 100 and 300 mg/kg/d groups, respectively. As discussed above, this was considered to be vehicle-related maternal toxicity, and RAC did not consider it to be treatment-related.

Structural abnormalities

In the prenatal developmental toxicity study in rats, 1997a, HHCB was administrated by gavage from gestation day 7 to 17. In this study, variations and malformations were observed in rats with a slight maternal toxicity. There were statistically significant increases in the litter and foetal incidences of overall malformations observed at the top dose (500 mg/kg bw/d). Malformations occurred in 1, 0, 2 and 6 foetuses from 1, 0, 2 and 5 litters in the control, 50, 150 and 500 mg/kg bw/d dosage group, respectively.

Multiple related head malformations (micrognathia, microcephaly, domed head, microphthalmia, absent or small tongue and/or eye bulge depressed or absent) occurred in one foetus of the control group, one or more of these malformations also occurred in one foetus of the mid-dose group and four foetuses from four different litters of the high dose group. Occurrences at the top dose were outside the range of the HCD. The interrelated craniofacial malformations observed in rats were considered by RAC to be treatment-related. Effects occurred in the absence of maternal toxicity.

In addition, in the DRF study (1997b) one foetus at 500 mg/kg bw/d also had micrognathia associated with low set ears and spina bifida.

Statistically significant increases in foetal incidences of thoracic vertebral malformations (hemivertebrae and centrum fused) associated with rib alterations were observed in the high dose group in 3 foetuses from 3 different litters. This finding was considered by RAC to be treatment-related.

Statistically significant increases in foetal incidences of incomplete ossification and/or no ossification of sternal centra and a significantly decreased number of ossification sites in the metatarsals were seen at 500 mg/kg bw/d.

Overall, RAC considered the occurrence of rare and severe craniofacial malformations to be treatment-related and not secondary to maternal toxicity. They considered these findings to be the most severe with regards to their relevance for classification.

Craniofacial malformations were also observed in the rabbit PNDT (2020), with one pup at 500 mg/kg bw/d with cleft palate (out of 157 in total), and another at the same dose with micrognathia, low set ears and spina bifida. As the incidence of this finding was small, RAC concluded that it was difficult to attribute it solely to treatment. Craniofacial malformations were not reported in the EOGRTS, although RAC noted that the top dose level in this study, 150 mg/kg bw/d, was lower than the top dose in both PNDTs.

Altered growth

Altered growth and development were both observed in rats in the prenatal developmental toxicity study and the EOGRTS.

In the prenatal developmental toxicity study in rats, there was a statistically significantly reduced pup body weight at the top dose (500 mg/kg bw/d) accompanied by a delay in ossification or absence of ossification in the absence of general maternal toxicity.

In the EOGRTS, the decrease in body weight was less pronounced in lactating dams compared to decrease in pup weight. In the F0-generation, during the lactation period, there was no effect on the body weight of the dams, while there was a statistically significant decrease in F1-pup body weight at the top dose from the start to the end of lactation.

The effects on the weight of male reproductive organs were more pronounced in the F1 generation than in the F0 generation, with a statistically significant decrease in absolute testis weight in top-dose F1 animals but an increase in relative weight in the mid and top dose. These changes were not associated with histopathological findings, and RAC did not consider them relevant for classification.

A decrease in AGD was observed at the mid and top dose in F2 males and females. However, as discussed above, RAC noted that the mean AGD at both of these doses fell within HCD ranges, and did not follow the pattern expected to occur as a result of an anti-

androgenic mechanism of action. Therefore, RAC concluded that this effect was of limited relevance for classification.

Functional deficiency

No effects on motor activity were noted in the peri/postnatal developmental neurotoxicity study, although RAC noted that this study could have been conducted at higher doses.

Conclusion

Overall, RAC concluded that there was clear evidence that HHCB induced adverse developmental effects in rats, based on findings of skull/craniofacial malformations in the OECD TG 414 rat study. These findings were supported by one incidence of micrognathia in the associated DRF and one incidence of cleft palate in the rabbit OECD TG 414 study. Classification was further supported by the statistically significant reduction in pup body weight in the rat OECD TG 414 study, and the decreased pup body weights during lactation in the F1 and F2 generations of the EOGRTS.

Therefore, RAC concluded that HHCB met the criteria for classification as Repr. 1B; H360D (May damage the unborn child).

Effects on or via lactation

For consideration of potential effects of HHCB on or via lactation, 2 studies and a group of biomonitoring reports were available.

RAC referred to table 54 in the CLH report, which provides an overview of available data from human biomonitoring studies dating from 1995-2006. These studies demonstrated the presence of HHCB in human milk. The concentrations of HHCB ranged from 10s-1000s µg/kg milk fat.

RAC made particular note of a toxicokinetic study by Hawkins *et al*., 1996a. In this study with pregnant and lactating rats, it was demonstrated that HHCB and its metabolites were transferred to milk. HHCB levels in mother's milk up to 2.28 and 32.8 mg HHCB equivalents/ml milk were found at oral doses of 2 and 20 mg 14C-HHCB/kg bw/d, respectively, were administered to dams.

Extended One Generation Reproductive Toxicity Study (EOGRTS), OECD TG 433, Wistar rats

The first study available for consideration of potential lactation related effects was the EOGRTS on Wistar rats described previously in this document. Groups of 25 Wistar rats/sex/dose group were administered HHCB at 470, 825 and 1650 ppm, equating to 42.5, 75 and 150 mg/kg bw/d. The EOGRTS was conducted with cohorts 1A, 1B and 1C but without DIT/DNT cohorts. The F1 generation was mated to produce the F2 generation.

The lactation index (calculated as number of pups alive on PND21/number of pups alive on PND4 (after culling) x 100) was not affected in either generation.

At the start of the lactation period for F0 animals, dams in the top dose group had a statistically significant decrease in body weight ↓ 7% on lactation day 1. At the end of the lactation period (lactation day 21) there was a statistically significant decrease in body weight in dams at the top dose ↓ 4.5% when compared with concurrent controls.

In the top dose group, 150 mg/kg bw/d, there was a statistically significant decrease in pup body weight from the start to the end of lactation ↓ 11%). The F1-generation continued to exhibit a dose-related reduction in mean body weight throughout the entire exposure period.

Statistically significant reductions in pup body weight were observed in the mid and top dose groups of both generations. In top dose F1 animals, these reductions were observed from PND 1 (↓8% compared to the control) and continued through to PND21 (↓11%). The reduction in mid-dose pup body weight was only statistically significant on PND21 in this generation (↓5.1%). In the F2 generation, pup body weights on PND7, 14 and 21 were statistically significantly reduced by 5%, 7% and 7%, respectively, at the mid dose and 7%, 13% and 11%, respectively at the top dose. As pup body weights were reduced from PND 1 in the F1 generation, and the foetal body weight reductions were observed in the rat PNDT study, RAC concluded that it was difficult to determine whether the body weight reduction was a result of exposure *in utero* or via lactation.

The DRF for the EOGRTS (2020a) was also available for evaluation, but RAC did not include it in their assessment, with the DS noting that it was difficult to draw comparisons from this study owing to a lack of control data.

Comparison to the classification criteria

According to Annex I, Table 3.7.1 (b) of the CLP Regulation, adverse effects on or via lactation are considered as a separate single category. Substances which are absorbed by women and have been shown to interfere with lactation, or which may be present (including metabolites) in breast milk in amounts sufficient to cause concern for the health of a breastfed child, shall be classified and labelled to indicate this property hazardous to breastfed babies. This classification can be assigned on:

- ‘human evidence indicating a hazard to babies during the lactation period; and/or
- results of one or two generation studies in animals which provide clear evidence of adverse effect in the offspring due to transfer in the milk or adverse effect on the quality of the milk; and/or
- absorption, metabolism, distribution and excretion studies that indicate the likelihood that the substance is present in potentially toxic levels in breast milk’.

RAC noted that the effects on pup body weight in the EOGRTS were not accompanied by other effects during lactation, and that it could not be determined whether they were caused by exposure to HHCB *in utero* or during lactation. Therefore, they concluded that classification for effects on or via lactation was not warranted.

Classification proposed by the Agency:

The Agency agrees with RAC's conclusion on classification. **HHCB meets the classification criteria for Repr. 1B; H360D (May damage the unborn child).** Classification is not warranted for adverse effects on sexual function and fertility or effects on or via lactation.

Aspiration hazard

Not assessed in the CLH report or RAC opinion.

Environmental hazards

Hazardous to the aquatic environment

Not assessed in the CLH report or RAC opinion.

Other hazards

Hazardous to the ozone layer

Not assessed in the CLH report or RAC opinion.

Overall conclusion

The Agency has evaluated the RAC Opinion, its rationale and any additional scientific evidence that may have been made available to HSE against the criteria for classification and labelling in the GB CLP Regulation and technical guidance.

The Agency technical report **agrees** with the classification proposed by RAC for the following hazards:

Repr. 1B; H360D (May damage the unborn child).

Overall, the conclusion is to **agree** with the RAC opinion.

References

ECHA (2024) Guidance on the Application of the CLP Criteria, Part 3: Health Hazards. Guidance to Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures, version 5.0, ref: ECHA-24-G-06-EN. Available at https://www.echa.europa.eu/

For all other references, please see the EU CLH report and the EU RAC opinion (available at: https://echa.europa.eu/registry-of-clh-intentions-until-outcome)

CLH (2024) CLH report (including Annexes): Proposal for Harmonised Classification and Labelling Based on Regulation (EC) No 1272/2008 (CLP Regulation), Annex VI, Part 2. Substance Name: 1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylindeno[5,6-c]pyran; [galaxolide]; [HHCB]; Date: 2024; Written by: France; Accessed date: 06/2026

ECHA (2026) Committee for Risk Assessment (RAC) Opinion (including Annexes) proposing harmonised classification and labelling at EU level of 1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylindeno[5,6-*c*]pyran; [galaxolide]; [HHCB]; Reference CLH-O-0000007605-71-01/F; Date: 25/03/2026; Accessed date: 06/2026

Documents published as part of the EU CLH process: Source: European Chemicals Agency, http://echa.europa.eu/

Glossary of terms used in Agency technical reports

Agency, the	HSE, acting in its capacity as the GB CLP Agency
AGD	Anogenital distance
AR	Applied radioactivity
ATE	Acute toxicity estimate
BCF	Bioconcentration factor
BOD	Biological Oxygen Demand
bw	Body weight
CAR	Competent Authority Report
CAS	Chemical Abstracts Service
CI	Confidence interval
CL	Confidence limits
CLH	Harmonised Classification and Labelling
CLP	Classification, labelling and packaging (of substances and mixtures)
CO_2	Carbon dioxide
COD	Chemical Oxygen Demand
CV	Coefficient of Variation
d	Day
DAR	Draft Assessment Report
DOC	Dissolved Organic Carbon
DRF	Dose range-finding
DS	Dossier Submitter
DT	Dissipation time OR degradation time (also DissT or DegT where apparent)
DT_{50}	Dissipation half-life OR degradation half-life (hours or days), see also above
dw	Dry weight
ECHA	European Chemicals Agency
ECx	x% effect concentration
EFSA	European Food Safety Authority
E_rCx	x% effect concentration based on growth rate
EOGRTS	Extended One-Generation Reproductive Toxicity Study
EU	European Union
GLP	Good Laboratory Practice
h	Hours
HCD	Historical control data
HHCB	1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylindeno[5,6-c]pyran; [galaxolide]; [HHCB]

K_{OC}	Organic carbon-water partition coefficient
K_{OW}	Octanol-water partition coefficient
LC_x	x% lethal effect concentration
LD	Lactation day
MCL	Mandatory Classification and Labelling
M-factor	Multiplying factor
MW	Molecular weight
MTD	Maximum Tolerated Dose
NOEC	No-observed effect concentration
NZW	New Zealand White
OECD	Organisation for Economic Co-operation and Development
PND	Post-natal day
PNDT	Pre-natal developmental toxicity
QSAR	Quantitative structure-activity relationship
RAC	Risk Assessment Committee
RAR	Renewal Assessment Report
RCOM	Response to comments document
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals regulation
STOT-RE	Specific target organ toxicity – repeated exposure
STOT-SE	Specific target organ toxicity – single exposure
TG	Test Guideline
US EPA	United States Environmental Protection Agency
wt	Weight
wwt	Wet weight

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